Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-44 are pending in the application, with claims 1-4, 13, 23, and 34 being the independent claims. Claims 7-10 are sought to be canceled without prejudice to or disclaimer of the subject matter recited therein. Claims 1-6 and 11-12 are withdrawn from further consideration. New claims 13-44 are sought to be added.

New claims 13, 23, and 34 are directed to the subject matter of cancelled claims 7-10 and are redrafted forms of these cancelled claims. Specifically, new claim 13 is directed to the subject matter of cancelled claims 7 and 8. New claims 14-22, which depend either directly or indirectly from new claim 13, are directed to specific embodiments of the new claim 13. Support for new claims 13-22 can be found in the specification, *inter alia*, at page 26, line 14, to page 29, line 21; at page 45, lines 5-28; and in Example 3 at page 51, line 20, to page 52, line 18.

New claim 23 is directed to the subject matter of cancelled claims 7 and 9. New claims 24-33 depend either directly or indirectly from new claim 23 and are directed to specific embodiments of new claim 23. Support for new claims 23-33 can be found in the specification, *inter alia*, at page 29, line 22, to page 31, line 20; at page 61, lines 4-31; and in Examples 7-9, at pages 65-70.

New claim 34 is directed to the subject matter of cancelled claims 7 and 10. New claims 35-44, which depend either directly or indirectly from new claim 34, are directed to specific embodiments of new claim 34. Support for new claims 34-44 can be found in the specification, *inter alia*, at page 31, line 21, to page 33, line 25.

New claims 13-33 read upon one or more elected species of the elected invention. New claims 13-33 read upon the elected species human polypeptide CYK-4, set forth in SEQ ID NO:2. New claims 13-22 read upon the elected species human RhoA, and new claims 23-33 read upon the elected species human MKPL1. New claims 23-33 read upon the elected species of a candidate compound's ability to interfere with the biochemical interaction of CYK-4 and a member of the MLKP1 protein subfamily.

These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and objections and that they be withdrawn.

I. The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph

The Examiner rejects claims 7-9 under 35 U.S.C. § 112, second paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. (Office Action, at page 4, paragraph 7, line 11-14.) Applicants respectfully traverse this rejection.

Specifically, the Examiner states:

> Claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying a modulator of human CYK-4 of SEQ ID NO:2 by determining the compound's ability to promote GTP hydrolysis by human Rho and to inhibit the binding of the human CYK-4 and human MKLP1, does not reasonably provide enablement for (i) a method for identifying a compound capable of modulating cytokinesis

> using ***fragments or variants*** of human CYK-4 of SEQ ID NO:2; (ii) a method for identifying a compound capable of modulating cytokinesis by measuring the compound's ability to modulate ***the function of CYK-4***; and (iii) a method for identifying a compound capable of modulating cytokinesis by measuring the compound's ability to ***interfere with the biochemical interaction*** of CYK-4 and a member of the MKLP1 subfamily.

(Office Action, at page 4, paragraph 7, lines 1-11.) (emphasis in original) The Examiner concludes that "the instant disclosure fails to enable the screening methods encompassed by the instant claims" and that "[i]t would require undue experimentation for one skilled in the art to make and use the claimed invention." (Office Action, at page 7, lines 16-18.)

In order to satisfy 35 U.S.C. § 112, first paragraph, Applicants must provide sufficient guidance so that one of ordinary skill in the art can make and use the claimed invention. The amount of enabling disclosure much be such that a person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In determining whether a patent application satisfies the enablement requirement under 35 U.S.C. § 112, first paragraph, the Federal Circuit held that "[e]nablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, 858 F.2d 731, 736-737 (Fed. Cir. 1988). However, the experimentation cannot be undue. *Id.* The Federal Circuit also held that "[t]he determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art." *Id.* at 737 (quoting *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. Pat. App. 1982)). The court states that "[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question

provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.*

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have cancelled claims 7-9, rendering moot the Examiner's rejection of these claims. New claims 13-33 are directed to the subject matter of cancelled claims 7-9, with new claims 13 and 23 reciting methods for identifying a compound capable of modulating cytokinesis comprising determining a compound's ability, respectively, to modulate the ability of a CYK-4 GTPase activating protein (GAP) or fragment thereof to promote GTP hydrolysis by a Rho family GTPase, and to interfere with the ability of a CYK-4 GAP or fragment thereof to interact with a member of the MKLP1 subfamily of kinesin-like proteins.

Applicants assert that they have provided sufficient guidance for one of ordinary skill in the art to make and use the claimed invention without undue experimentation and that the present application enables the full scope of the claims as presently amended.

The Examiner states, at page 5 of the Office Action, that "[t]he claims encompass a method using any fragments or variants of human CYK-4 of SEQ ID NO:2 . . . ." and that "[t]here is no disclosure of any fragments or variants of SEQ ID NO:2 that retains the activity of SEQ ID NO:2." (Office Action, at page 5, lines 8-9 and 15-16.) The Examiner further states:

> [T]he specification fails to provide sufficient direction or working examples on how to make modulators of cytokinesis using variants and fragments of human CYK-4 polypeptide of SEQ ID NO:2. One skilled in the art would first have to determine the activity of fragments or variants of human CYK-4 polypeptide of SEQ ID NO:2 in order to develop the claimed assay. While providing a number of active fragments of murine CYK-4 of SEQ ID NO:4, which

> shares 84.3% sequence identity with SEQ ID NO:2, the specification provides no guidance specific to the fragments and variants of SEQ ID NO:2. For example, the specification is silent with respect to which amino acid residues or regions are critical for promoting GTP hydrolysis by a Rho family GTPase and for the binding of CYK-4 of SEEQ [sic] ID NO:2 and human MKLP1, and which residues may be altered without loss of activity.

(Office Action, at page 6, line 13, to page 7, line 1.) The Examiner summarizes by stating that "[t]he information available in the art and disclosed in the instant specification . . . would not be sufficient to help to predict whether a variant or fragment of human CYK-4 polypeptide of SEQ ID NO:2 retains the activity of SEQ ID NO:2 and can be used in the claimed screening assay . . . ." and that "it would take undue experimentation for one skilled in the art to make and use the claimed method." (Office Action, at page 7, lines 8-14.)

As noted previously, Applicants have cancelled claims 7-9, rendering moot the Examiner's rejection of these claims, and have added new claims 13-33, directed to the subject matter of cancelled claims 7-9. Applicants note that new claims 13-33 recite a fragment of CYK-4, and new claims 25-33 recite a fragment of MKLP1.

Contrary to the Examiner's statements, the current specification provides ample guidance on how to make the CYK-4 (and MKLP1) fragments of the invention. For example, at 50, lines 22, the specification describes several domains of *C. elegans* CYK-4 that are shared by mouse, human, and Drosophila forms of CYK-4 and are thus conserved among metazoans: a conserved C-terminus containing a GTPase activating protein (GAP) domain; a C1 domain predicted to bind to diacylglycerol or phorbol esters; and an amino terminal coiled-coil domain that mediates the interaction of CYK-4 with ZEN-4/MKLP1 (see also page 14, line 18, to page 15, line 11; and page 31, lines 2-5). Fig. 3 D, moreover,

illustrates the correspondence of conserved domains between the *C. elegans* CYK-4 protein and human CYK-4, indicating which amino acid residues or regions are critical for promoting GTP hydrolysis by a Rho family GTPase and for the binding of CYK-4 of human CYK-4 and human MKLP1. Contrary to the Examiner's comment, the specification, in Fig. 3D, clearly indicates for human CYK-4 the amino-terminal coiled coil region critical for CYK-4/MKLP1 binding and the C-terminal GAP domain critical for GTPase activating activity. Lastly, the specification indicates the region of the ZEN-4/MKLP1 protein that binds to CYK-4 and states that this region of ZEN-4/MKLP1 – the linker region – is conserved in members of the MKLP1 subfamily of kinesin-like proteins. See the specification at page 14, line 29, to page 15, line 6; at page 30, line 24, to page 31, line 9; and in Example 9, at pages 69-70.

Thus, contrary to the Examiner's statement, with the information provided in the current specification, one of skill in the art would be able to predict which amino acid residues and regions are critical for the CYK-4/MKLP1 binding interaction and the CYK-4 GAP activity of the claimed methods.

The specification also provides guidance on how to make and use CYK-4 (and MKLP1) fragments through the detailed descriptions of the CYK-4 (and ZEN-4/MKLP1) fragments and their use in binding assays presented in the specification. See the specification, at page 61 and in Examples 8-9, at pages 67-70. Methods for producing such fragments are well known in the art. See, for example, page 22, line 25, to page 23, line 14, of the specification, and the treatise cited therein, at page 22, line 29 (Sambrook *et al.*, 2000, Molecular Cloning, (Third Ed.)). The Sambrook treatise, which is cited in the specification as a reference (see page 93), is a manual well-known to those of skill in the

art that provides detailed descriptions of molecular biological techniques that can be used to produce the CYK-4 (and MKLP1) fragments of the claimed methods.

Applicants also note that a polypeptide "fragment" is defined in specification at page 23, lines 6-11, as a polypeptide comprising at least 15, and more preferably at least 20, contiguous amino acids of a reference polypeptide (for example, SEQ ID NO:2). The specification, at page 23, lines 20-31, also describes CYK-4 polypeptides variants or derivatives as polypeptides which have sequences that deviate from a reference CYK-4 polypeptide (such as that in SEQ ID NO:2 or 4, caused by conservative exchange of amino acids, if the derivatives have properties which are desirable for their use in therapy or in screening assays. Such variants or derivatives could be easily made by those of skill in the art without undue experimentation.

Furthermore, contrary to the Examiner's statements that there are no disclosures of any fragments or variants of human CYK-4 that retain the activity of CYK-4, Applicants note that it is long settled case law that Applicants are not required to provide objective evidence in the form of working examples to enable the claimed invention. In *In re Marzocchi*, 439 F.2d 220, 223 (C.C.P.A. 1971), the court stated that "[t]he first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance."

Moreover, with respect to the Examiner's statement that one skilled in the art would first have to determine the activity of fragments or variants of human CYK-4 polypeptides in order to develop the claimed assay, Applicants further note that, as discussed previously, the current specification provides sufficient guidance as to which regions and amino acids

of human CYK-4 retain GAP and CYK-4/MKLP1 binding domains. Creation of fragments of human CYK-4 containing these respective domains, with their respective GAP CYK-4 binding activities necessary for the claimed screening assays, would be routine to one of skill in the art and not require undue experimentation.

Thus, contrary to the Examiner's statement, it would not take undue experimentation for one skilled in the art to make and use the CYK-4 fragments of the claimed methods. However, in order to advance the prosecution of the present application and without acquiescence to the rejection, new claims 13 and 23 have been drafted to recite that the specific CYK-4 GAP fragment of the claim comprises, respectively, a GAP domain or a domain that interacts with an MKLP1 protein. New claim 30 also recites specific amino acids present in some of the claimed CYK-4 fragments.

The Examiner also states, at page 5 of the Office Action, that "the claims encompass a method . . . measuring any functions of CYK-4, and determining any biochemical interaction of CYK-4 and a member of the MKLP1 subfamily" and that "the specification merely discloses a method for identifying a modulator of human CYK-4 of SEQ ID NO:2 by determining the compound's ability to promote GTP hydrolysis by human Rho and to inhibit the binding of the human CYK-4 and human MKLP1." (Office Action, at page 5, lines 8-14.) The Examiner further states that "[t]here is no disclosure of a method for identifying modulators of cytokinesis by determining other biological functions." (Office Action, at page 5, lines 16-17.)

In order to advance the prosecution of the present application and without acquiescence to the rejection, new claims 13 and 23 have been drafted to recite specific methods for identifying a compound capable of modulating cytokinesis, *i.e.*, those

comprising determining a compounds' ability, respectively, to modulate the ability of a CYK-4 GTPase activating protein (GAP) or fragment thereof to promote GTP hydrolysis by a Rho family GTPase, and to interfere with the ability of a CYK-4 GAP or fragment thereof to interact with a member of the MKLP1 subfamily of kinesin-like proteins.

Also, in order to advance the prosecution of the present application and without acquiescence to the rejection, new claim 23 has been drafted to recite a method that comprises determining the ability of a compound to interfere with the ability of a CYK-4 GAP "to interact with" an MKLP1 protein. Thus, the phrase "to interfere with the biochemical interaction of" in cancelled claim 9 has been replaced with the phrase "to interact with" in new claims 23 and 24.

Applicants have provided sufficient guidance for one of ordinary skill in the art to make and use the claimed invention without undue experimentation. The present application thus enables the full scope of the claims as presently amended. Accordingly, Applicants assert that the rejection of claims 7-9 under 35 U.S.C. § 112, first paragraph, has been overcome and respectfully request the Examiner to reconsider and withdraw this rejection.

II. The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph

The Examiner also rejects claims 7-9 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (Office Action, at page 8, paragraph 9.)

Specifically, the Examiner states that "the steps of the methods do not necessarily achieve the goal set forth in the claim preamble. It is unclear how a candidate modulator is selected, determined, and correlated to the preamble." (Office Action, at page 8, lines 5-7.)

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have cancelled claims 7-9, rendering moot the Examiner's rejection of these claims.

Applicants, however, note that new claims 13-33 are directed to the subject matter of cancelled claims 7-9. New claims 14 and 24 each recite steps for the methods recited in new claims 13 and 23, respectively, which correspond to cancelled claims 7-9. Moreover, each of new claims 14 and 24 recites language that correlates the recited steps in the claim to the preamble of the claim.

The Examiner further states that claims 7-9 "recite the terms 'CYK-4' and 'MKLP1'. Such acronyms are determined arbitrarily and may change with time. For clarity, it is suggested that the terms be spelled out in each independent claim" and that "CYK-4 be modified by SEQ ID NO:2 for clarity." (Office Action, at page 8, lines 11-14.)

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have cancelled claims 7-9, rendering moot the Examiner's rejection of these claims. Applicants note, however, that new independent claims 13 and 23 each recites language supported by the specification that, in addition to the acronyms identifying CYK-4 and/or MKLP1, describes each of the proteins. For example, new independent claims 13 and 23 each recites "a CYK-4 GTPase activating protein (GAP)." New claim 23 recites "a member of the MKLP1 subfamily of kinesin-like proteins." Moreover, in new claims that

explicitly recite human CYK-4, the identifying phrase "SEQ ID NO:2" is recited as well. See, for example, new claims 16 and 17.

Lastly, the Examiner states that "claim 7 recites the term 'the function of CYK' whereas claim 9 recites 'the biochemical interaction'. Neither the art nor the specification provides an unambiguous definition for the terms. . . . For example, it is unclear what biochemical interaction else, in addition to binding is encompassed in claim 9." (Office Action, at page 8, lines 15-19.)

To expedite prosecution and without acquiescing in the propriety of the rejection, Applicants have cancelled claims 7-9, rendering moot the Examiner's rejection of these claims. Applicants note that in new claims 23 and 24, "biochemical interaction" has been replaced with "interaction." The term 'interaction' is used throughout the specification to indicate binding and/or association in a complex. See, for example, the specification at page 30, lines 26-28; at page 31, line 21, to page 33, line 8; a page 67, lines 15-18; at page 69, lines 16-19; and at page 71, lines 4-21.

Applicants assert that the rejection of claims 7-9 under 35 U.S.C. § 112, second paragraph, has been overcome and respectfully request the Examiner to reconsider and withdraw this rejection.

III. The Objections to the Claims – Minor Informalities

The Examiner objects to claims 7-9 as reciting unelected subject matter and states that "[a]ppropriate correction is required." (Office Action, at page 8, paragraph 10.)

To expedite prosecution and without acquiescing in the propriety of the objection, Applicants have cancelled claims 7-9, rendering moot the Examiner's objection to these claims.

Where possible, cancelled claims 7-9 have been redrafted to recite only elected subject matter in new claims 13-33. See, for example, new independent claim 23 and new dependent claims 19 and 27. However, Applicants note that generic claims, *i.e.*, those reciting more than one elected species, are permitted in an application during prosecution, after an election of species has been made. See, for example, the Manual of Patent Examining Procedure (MPEP), at §§ 809.02(e) and 809.03 (August 2001).

Accordingly, the objection to claims 7-9 has been overcome and Applicants respectfully request that the objection be withdrawn.

IV. Other Matters - The Information Disclosure Statement

The Examiner states that although U.S. PTO records indicate that Applicants submitted an Information Disclosure Statement for the captioned application on January 8, 2002 (US PTO Prosecution File Wrapper Paper No. 6), the Examiner has not been able to locate the Information Disclosure Statement. Accordingly, the Examiner requests that Applicants resubmit a copy of the Information Disclosure Statement and the cited references submitted earlier.

Further to the Examiner's request, Applicants submit herewith copies of the Information Disclosure Statement, form PTO-1449, and references cited therein that were submitted to the US PTO on January 18, 2002. (Applicants respectfully note that their

records indicate that the Information Disclosure Statement for the captioned application was filed on January 18, 2002.)

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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